

# The erythromycin PKS

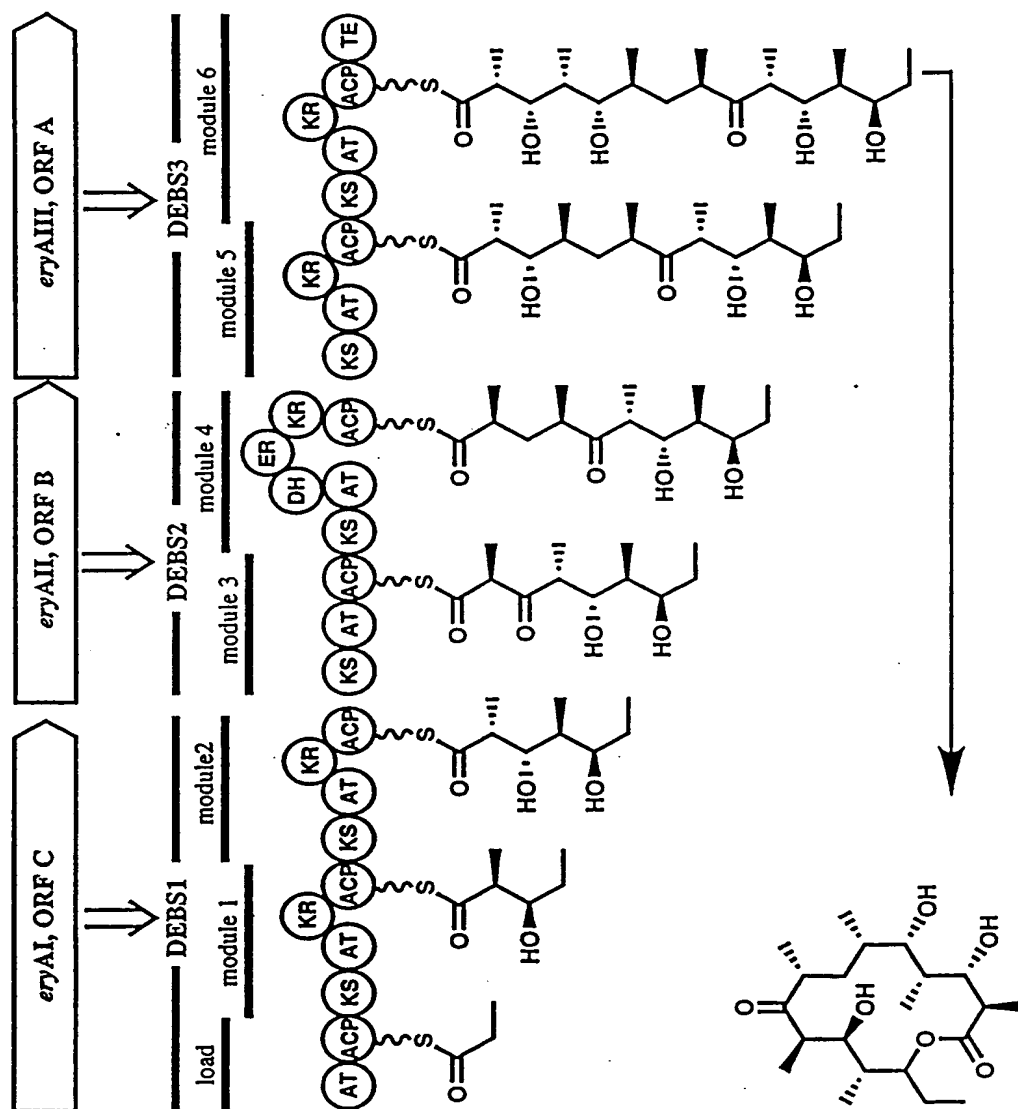


Fig. 1

2/12

KCLFDAU  
KCLFPEU  
KCLFACT  
KCLFHIR  
KCLFGRA  
KCLFNOG  
KCLFTCM  
KCLFCIN  
KCLFVNZ  
KCLFWHIE  
KSGRA  
KSHIR  
KSACT  
KSCIN  
KSVNZ  
KSNOG  
KSTCM  
KSDAU  
KSPEU  
KSWHI

-----MVTGLGIVAPNGLGVGAIWDAVLNGRNGIGPLR  
MTGTAARTASSQLHASPAGRRGLRGRAVVTGLGIVAPNGLGVGAYWDAVLNGRNGIGPLR  
-----MSVLTITGVGVVAPNGLGLAPYWSAVLDGRHGLGPVT  
-----MSTWVTGMGVVAPNGLGADDDHWAATLKGRHGHSRLS  
-----MSTPDRRRRAVVTGLSVAAPGGLGTERYWKSLTGENGIAELS  
-----MTAAVVVTGLGVVAPTGLGVREHWSSTVRGASAI GPVT  
-----MSAPAPVVVTGLGIVAPNGTGTTEEYWAATLAGKSGIDVIQ  
-----MTP-VAVTGMGLAAPNGLGRPTTGRPPWAPRAASAAS  
-----MSASVVVTGLGVVAPNGLGREDFWASTLGGKSGIGPLT  
-----MSGPQRTGTGGSSRAVVTGLGVLSPHGTGVEAHKAVADGTSSLGPVT  
-----MTRRVVITGVGVRAPGGSGTKEFWDLLTAGRTATRPIS  
-----MTRRVVITGVGVRAPGGGAKNFWELLTSGRTATRRIS  
-----MKRRVVITGVGVRAPGGNGTRQFWELLTSGRTATRRIS  
-----MTQRRVAITGIEVLAPGGLGRKEFWLLTSEGRATRGIT  
-----MTARRVVITGIEVLAPGGTGSKAFWNLLSEGRATRGIT  
-----MKESINRRVVITGIGIVAPDATGVKPFWDLLTAGRTATRTIT  
-----MIRHAEKRVVITGIGIVRAPGGAGTAAFWDLLTAGRTATRTIS  
-----MNRRVVITGMGVVAPGAIGIKSFWELLTSGTTATRAIT  
-----MNRRIVITGIGVVAPGAVGTPKFWELLTSGTTATRAIS  
-----MTRRRVAVTIGIVVAPGGIGTPQFWRLTSEGRATRRIS

:\*: : : \*

KCLFDAU  
KCLFPEU  
KCLFACT  
KCLFHIR  
KCLFGRA  
KCLFNOG  
KCLFTCM  
KCLFCIN  
KCLFVNZ  
KCLFWHIE  
KSGRA  
KSHIR  
KSACT  
KSCIN  
KSVNZ  
KSNOG  
KSTCM  
KSDAU  
KSPEU  
KSWHI

RFADDGRLGRLAGEVSDFVP-EDHLPKRLLVQTDPMIQTALAAAEWALREAGCAPSS--  
RFTGDGRLGRLAGEVSDFVP-EDHLPKRLLAQTDPMIQTALAAAEWALREAGCAPSS--  
RFDVSRYPATLAGQIDDFHA-PDHI PGRLLPQTD PSTRL-ALTAADWALQDAKADPES-L  
RFDPTGYPAELAGQVLDFA-TEHLPKRLLPQTDVSTRF-ALAAADWALADAGVGPESGL  
RFDASRYPSRLAGQIDDFEA-SEHLPKRLLPQTDVSTRY-ALAAADWALADAGVGPESGL  
RFDAGRYPSKLAGEVPGFVP-EDHLPKRLLPQTDHMTL-ALVAADWAFQDAAVDP SK-L  
RFDPHGYPVRVGGEVLAFDA-AAHLPGRLLPQTDRTQH-ALVAAEWALADAGLEPEK-Q  
RFDPSGYPAQLAGEIPGFRA-AEHLPGRLVPQTDRTVTRL-SLAAADWALADAGVEVAA-F  
RFDPTGYPARLAGEVPGFAA-EEHLPKRLLPQTDRTMTRL-ALVAADWALADAGVRPEE-Q  
REGCAHLPLRVAGEVHGFA-AETVEDRFLVQTDRTFTHF-ALSATQHALADARFGRADVD  
FFDASPFRSRIAGEI-DFDAVAEGFSPREVRMDRATQF-AVACTRDALADSGLD TGA-L  
FFDPTPNRSQIAAEC-DFDPEHEGLSPREIRMDRAAQF-AVCTRDADADSGLEFEQ-V  
FFDPSPYRSQVAAEA-DFDPVAEGFGPRELDRMDRASQF-AVACAREAFASGLDPDT-L  
FFDPAPFRSKVAAEA-DFCGLNGLSPQEVRRMDRAAQF-AVV TAR-AVEDSGAELAA-H  
FFDPTPFRSRVAAEI-DFDPEAHGLSPQEI RMDRAAQF-AVVAAR-AVADSGIDLAA-H  
AFDPSPFRSRIAAEC-DFDPLAEGLTPOQIRMDRATQF-AVVSARESLED SGLDLGA-L  
LFDAAPYRSRIAGEI-DFDPIGEGLSPQASTYDRATQL-AVVCAREALKDSGLDPAA-V  
TFDATPFRSRIAAEC-DFDPVAAGLSAEQARRLDRAQF-ALVAGQEALD SGLRIGE-D  
TFDATPFRSRIAAEC-DFDPVAAGLSAEQARRLDRAQF-ALVAGQEALD SGLRIGE-D  
LFDPSGLRSQIAAEC-DFEPSDHGLGLATAQRCDRYVQF-ALVAASEAVRDANLDMNR-E

:... : \* : : : : : :

Fig 2A

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KCLFDAU  
KCLFPEU  
KCLFACT  
KCLFHIR  
KCLFGRU  
KCLFNOG  
KCLFTCM  
KCLFCIN  
KCLFVNZ  
KCLFWHIE  
KSGRA  
KSHIR  
KSACT  
KSCIN  
KSVNZ  
KSNOG  
KSTCM  
KSDAU  
KSPEU  
KSWHI

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-PLEAGVITASASGGFASGQRELQNLWSKG-----PAHVSAYMSFAWFY-AVNTGQIAIR
-PLEAGVITASASGGFAFGQRELQNLWSKG-----PAHVSAYMSFAWFY-AVNTGQIAIR
TDYDMGVVTANACGGFDFTHREFRKLWSEG-----PKSVSVYVESFAWFY-AVNTGQISIR
PEYGTGVI TSNATGGFEFTHREFRKLWAQG-----PEFVSVYVESFAWFY-AVNTGQISIR
DDYDLGVVSTTAQGGFDFTHREFHKLWSQG-----PAYVSVYVESFAWFY-AVNTGQISIR
PEYLGVVVTTASSAGGFEGFHRELQNLWSLG-----PQVVSAYQSFAWFY-AVNTGQVSIR
DEYGLGVLTAAGAGGFEFGQREMOKLWGTG-----PERVSAYQSFAWFY-AVNTGQISIR
DPLDMGVVTASHAGGFEFGQDELQKLLGQG-----QPVL SAYQSFAWFY-AVNSGQISIR
DDFDMGVVTASASGGFEFGQDELQKLLWSQG-----SQVVSAYQSFAWFY-AVNSGQISIR
SPYSVGVVTAAGSGGGEGFGQRELQNLWGHG-----SRHVGPYQSIADWY-AASTGQVSIR
DPSRIGVALGSASAVATSLENEYLVMSDSGREWLVDPAHLSPMFDFYLSPGVMPAEVAWA
PPERIGVSLGSAAVAATSLEQEYLVLSDDGGREWQVDPAYLSAHMFDFYLSPGVMPAEVAWT
DPA RVGVSLGSAAVAATSLEREYLLSDSGRDWEVDAAWL SRHMFDFYLVPSVMPAEVAWA
PPHRIGVVVGS AVGATMGLDNEYRVVSDGGRLDLVDHRYAVPHLYNYLVPSSFAAEVAWA
DPYRVGVTVGS AVGATMGLDEEYRVVSDGGRLDLVDHAYAVPHLYDYFVPPSSFAEVAWA
DASRTGVVVGS AVGCTTSLEEYAVVSDSGRNWLVDGDYAVPHLFDYFVPPSSIAAEVAHD
NPERIGVSI GTAVGCTTGLEDREYARVSEGGSRWLVDHDTLAVEQLFDYFVPPSSIAAEVAWE
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SAHRVGVCVGTAVGCTQKLESEYVALSAGGAHVVDPGRGSELYDYFVPPSSLAAEVAWL
DPWRAGATLGTAVGGTTTRLEHDYVLVSEGRSRWDVDDRRSEPHLERAFTPATLSSAAVAEE
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KCLFDAU  
KCLFPEU  
KCLFACT  
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KCLFGRA  
KCLFNOG  
KCLFTCM  
KCLFCIN  
KCLFVNZ  
KCLFWHIE  
KSGRA  
KSHIR  
KSACT  
KSCIN  
KSVNZ  
KSNOG  
KSTCM  
KSDAU  
KSPEU  
KSWHI

-HDLRGPVGVVVAEQAGGLDALAHAR-RKVRGGAE-LIVSGAMDSSLCP-YGMAAQVRS  
-HDLRGPVGVVVAEQAGGLDALAHAR-RKVRGGAE-LIVSGAVDSSLCP-YGMAAQVKS  
-HGMRGPSSALVAEQAGGLDALGHAR-RTIRRGTP-LVVS GGVDSSALDP-WGWVVSQIASG  
-HGLRGP GSVLVAEQAGGLDAVGHG--AVRNGTP-MVVTGGVDSSFPD-WGWVSHVSSG  
-NIMRGP SAALVGEQAGGLDAIGHAR-RTVRRGPG-WCSAVASTRRSTR-GASSQLSGG  
-HGLRGP GGVLVTEQAGGLDALGQAR-RQLRRGLP-MVVGAVDGSFPCP-WGWVAQLSSG  
-HGMRGHSSVFVTEQAGGLDAAHAA-RLLRKGT LNTALTGGCEASLCP-WGLVAQIPSG  
-HGMKGP SGVVSDQAGGLDALAQAR-RLVRKGTP-LIVCGAVEPR SAPGAGSPSSPAGG  
-NGMKGP SGVVSDQAGGLDAVAQAR-RQIRKGTR-LIVSGGDASLCP-WGWVAHVASD  
-NDFKGP CGVVADEAGGLDALAHAA-LAVRNGTD-TVVCGATEAPLAP-YSIVCQLGYF  
-AGAEGPVTMVS DGTSGLDSVGYAV-QTRREGSADVVAGAADTPVSP IYVACFDAIKA  
-VGAEGPVMVMSDGTSGLDSL SHAC-SLIAEGTTDVMVAGAADTPITPIVVS CFDAIKA  
-VGAEGPVTM/STGCTSGLDSVGNV-RAIEEGSADVMFAGAADTPITPIVVS CFDAIRA  
-VGAEGPSTVSTGCTSGIDAVGLAV-ELVREGSVDVMVAGAVDAPISPIPCVLDAIKA  
-VGAEGPNTVSTGCTSGLDSVGYARGELIREGSADVMLAGSSDAPISPIITMACFDAIKA  
RIGAEGPVSLVSTGCTSGLDAVGRAA-DLIAEGAADVMLAGATEAPISPIITVACFDAIKA  
-AGAEGPVTVSTGCTSGLDAVGYGT-ELIRDGRADVVCATDAPISPIITVACFDAIKA  
-AGAEGPVNIVSAGCTSGIDSIGYAC-ELIREGTVDMVLAGVDAP IAPITVACFDAIRV  
-AGAEGPVNIVSAGCTSGIDSIGYAC-ELIREGTVDMVAGGV DAPIAPITVACFDAIRA  
-FGVRGPVQTVSTGCTSGLDAVGYAY-HAVAEGRVDVCLAGAADSPISPIITMACFDAIKA

KCLFDAU  
KCLFPEU  
KCLFACT  
KCLFHIR  
KCLFGRA  
KCLFNOG  
KCLFTCM  
KCLFCIN  
KCLFVNZ  
KCLFWHIE

RLSGSDPTAGYLPFDRRAAGHVPGE-GAILAVEDAERVAERG-GKVGSIAGT-ASF  
RLSGSDNPTAGYLPFDRRAAGHVPGE-GAILTVEDAERAAERG-AKVGSIAGYGASFD  
RISTATDPDRAYLPFDERAAGYVPGE-GAILVLEDSAAAEARGRHDAYGELAGCASTFD  
RVSRATDPGRAYLPFDVAANGYVPGE-GAILLLEDAESAKARG-ATGYGEIAGYAATFD  
LVSTVADPERAYLPFDVDASGYVPGE-GAVLIVEDADSARARG--AERIYVRSPLRRD  
GLSTSDDPRRAYLPFDAAAGGHVPGE-GALLVLESDESARARGVTRWYGRIDGYAATFD  
FLSEATDPHDAYLPFDRAAGHYVPGE-GAMLVAERADSARERDAATVYVRIAGHAATFD  
-MSDSDENRAYLPFDRDRGRYVPGGGRGVVPLERAEAAPARG-AEYVGE-AGPLARL-  
RLSTSEEPARGYLPFDREAQGHVPGE-GAILVMEAAEAARERG-ARIYGEIAGYGSTFD  
ELSRATEPDRAYRPFTEACGFAPAEG-GAVLVVEEEAAARERG-ADVTRATVAGHAATFT

Fig 2B

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KSGRA	TTPRNDDPAHASRPFDGTRNGFVLAEG-AAMFVLEEYEEAAQRRG-AHIYAEVGGYATRSQ
KSHIR	TTPRNDDPEHASRPFDNSRNGFVLAEG-AALFVLEELEHARARG-AHVYAEISGCATRLN
KSACT	TTARNDDPEHASRPFDGTRDGFVLAEG-AAMFVLEDYDSALARG-ARIHAEISGYATRCN
KSCIN	TTPRHDAPATASRPFDSTRNGFVLGEG-AAFFVLEELHSARRRG-AHIYAEIAGYATRSN
KSVNZ	TTNRYDDPAHASRPFDGTRNGFVLGEG-AAVFLLEELESARARG-AHIYAEIAGYATRSN
KSNOG	TTPRNTPAEASRPFDRTNGFVLGEG-AAVFLVEEFHARRRG-ALVYAEIAGFATRCN
KSTCM	TSANNDPAHASRPFDNRDGFVLGEG-SAVFVLEELSAARRRG-AHAYAEVRGFATRSN
KSDAU	TSDHNDTPETLA-PFSRSRNGFVLGEG-GATVVLEEAEAAVRRG-ARIYAEIGGYASRGN
KSPEU	TSDHNDTPETASRPFSRSRNGFVLGEG-GATVVLEEAEAAVRRG-ARIYAEIGGYASRGN
KSWHI	TSPNNDPAHASRPFDADRNCFVMGEG-AAVLVLEDLEHARARG-ADVCEVSGYATTFGN
	*        **        * . . . * . . . * . . . *
KCLFDAU	-PPPGSGRP---SALARAVETALADAGLDRSDIAVVFADGAA-VGELDVAAEAEALASVFG
KCLFPEU	-PPPGSGRP---SALARAVETALADAGLDGSDIAVVFADGAA-VPELDAAEAEALASVFG
KCLFACT	-PAPGSGRP---AGLERAIRLALNDAGTGPEVDVVFADGAG-VPELDAAEAEARIGRVFG
KCLFHIR	-PAPGSRP---PALRRRAIELALADAELRPEQVDVVFADAAG-VAELDAIEAAAI RELFG
KCLFGRA	-PAPGSGRP---PALGRAAEALALAEAGLTPADISVVFADGAG-VPELDRAEADTLARLFG
KCLFNOG	-PPPGSGRP---PNLLRAAQALDDAEVGP EAVDVVFADAG-TPEDAAEADAVRRLFG
KCLFTCM	-ARPGTGRP---TGPARAIRLALAEARVAPEVDVVFADAAG-VPALDRAEAEALAEVFG
KCLFCIN	-PAPHSGRG---STRAHAIRLALDDAGTAPGDIRRVFADGGGYPN-DRAEAEAI SEVFG
KCLFVNZ	-PRPGSGRE---PGLRKAI ELALADAGAAPGDIDVVFADAAA-VPELDRVEAEALNAVFG
KCLFWHIE	GAGRWAESR---EGLARAIQ GALAEAGCRPEEVDVVFADALG-VP EADRAEALALADALG
KSGRA	-AYHMTGLKKDGREMAESIRALDEARLDRTAVDYVNAHGSG-TKQNDRHETA AFKRS LG
KSHIR	-AYHMTGLKTDGREMAEAI RVALDLARIDPTDIDYINAHGSG-TKQNDRHETA AFKRS LG
KSACT	-AYHMTGLKADGREMAETIRVALDESRTDATDIDYINAHGSG-TRQNDRHETA AFKRS LG
KSCIN	-AYHMTGLR-DGAEMAEAIRLALDEARLNPEQVDYINAHGSG-TKQNDRHETA AFKRS LG
KSVNZ	-AYHMTGLRPDGAEMAEAI RVALDEARMNPTEIDYINAHGSG-TKQNDRHETA AFKRS LG
KSNOG	-AFHMTGLRPDGREMAEAI GVALAQAGKAPADVDYVNAHGSG-TRQNDRHETA AFKRS LG
KSTCM	-AFHMTGLKPDGREMAEAI TAALDQARRTGDDLHYINAHGSG-TRQNDRHETA AFKRS LG
KSDAU	-AYHMTGLRADGAEMAAAI TAALDEARRDP SDVDYVNAHGTA-TRQNDRHETS AFKRS LG
KSPEU	-AYHMTGLRADGAEMAAAI TAALDEARRDP SDVDYVNAHGTA-TKQNDRHETS AFKRS LG
KSWHI	-AYHMTGLTKEGLEMARAI DTALDMAELDGS AIDYVNAHGSG-TQQNDRHETA AVKRS LG
	. : : : ** : : : * . . . * * : : *

Fig 2c

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KCLFDAU  
KCLFPEU  
KCLFACT  
KCLFHIR  
KCLFGRA  
KCLFNOG  
KCLFTCM  
KCLFCIN  
KCLFVNZ  
KCLFWHIE  
KSGRA  
KSHIR  
KSACT  
KSCIN  
KSVNZ  
KSNOG  
KSTCM  
KSDAU  
KSPEU  
KSWHI

P--HRVPVTVPKLTGRLYSGAGPLDVATGLLALRDEVVPATGHVH-PDPDLPLDVVTGR  
P--RRVPVTVPKLTGRLYSGAGPLDVATALLALRDEVVPATAHVD-PDPDLPLDVVTGR  
R--EGVPVTVPKTTTGRLYSGGGPLDVVTALMSLREGVIAPTAGVTSVPREYGIDLVLGE  
P--SGVPVTAPKMTGRLYSGGGPLDLVAALLAIRDQVIPPVHTAEFVPEHQDLVTGD  
P--RGVPVTAPKALTGRLCAGGGPADLAAALLALRDQVIPATGRHRAVPDAYALDLVTGR  
P--YGVVTVAPKMTGRLSAGGAALDVATALLALREGVVPPTVNVSRPRPEYELDLVLA-  
P--GAVPVTAPKMTGRLYAGGAALDVATALLSIRDVVPPTVGTGAPAPGLGIDLVLHQ  
P--GRVPVTCPRMTGRLHSGAAPLDVACALLAMRAGVIPPVTHID-PCPEYDLDLVLYQ  
T--GAVPVTAPKMTGRLYSGAAPLDLAAFLAMDEGVIPTVNVE-PDAAYGLDLVVGG  
PHAARVPVTAPKTGTGRAYCAAPVLDVATAVLAMEHGLIPPTPHVL--DVCHDLDLVTGR  
EHAYAVPVSSI KSMGHS LGAGSIEIAASVLAIEHNVVPPTANLHTPDPECDLDYVPLT  
EHAYRTPVSSI KSMVGHSLGAGSIEVAACALAI EHGVPPTANLHEPDPECDLDYVPLT  
EHARRTPVSSI KSMVGHSLGAGSLEIAACVLALEHGVPPTANLRTSDPECDLDYVPLE  
EHAYRTPVSSI KSMVGHSLGAGSIEIAASALAMEYDVVPPTANLHTPDPECDLDYVPLT  
DHAYRTPVSSI KSMVGHSLGAGSIEIAASALAMEYDVVPPTANLHTPDPECDLDYVPLR  
DHAYRVPVSSI KSMIGHSLGAGSLEIAASVLAITHDVVPPTANLHEPDPECDLDYVPLR  
QRAYDVPVSSI KSMIGHSLGAGSLELAACALAI EHGVIPTANYEEDPECDLDYVPLT  
DHAYRVPVSSI KSMIGHSLGAGSLEVAATATAVEYGAIPPTANLHDPDPELDLDYVPLT  
EHAYRVPVSSI KSMIGHSLGAGSLEVAATATAVEYGVIPPTANLHDPDPELDLDYVPLT  
EHAYATPMSSI KSMVGHSLGAGSIEIAACVLA MAHQVVPPTANYTTPDPECDLDYVPRE  
\*:: :: \* . :::: :::: :::: ::::

KCLFDAU  
KCLFPEU  
KCLFACT  
KCLFHIR  
KCLFGRA  
KCLFNOG  
KCLFTCM  
KCLFCIN  
KCLFVNZ  
KCLFWHIE  
KSGRA  
KSHIR  
KSACT  
KSCIN  
KSVNZ  
KSNOG  
KSTCM  
KSDAU  
KSPEU  
KSWHI

PRAMADARAALVVARGHGGFNSALVVRGAA-----  
PRSLADARAALLVARGYGGFNSALVVRGAA-----  
PRSTAPRTA-LVLARGRWGFNSAAVLRRAFPTP----  
PRHQQLGTA-LVLARGKWGFNSAVVVRGVGT-----  
PREAALSAA-LVLARGRHGFNSAVVVTLRGSDHRRPT  
PRRTPLARA-LVLARGRGGFNAAMVVAGPRAETR---  
PRELRVDTA-LVVARGMGGFNSALVVRRHG-----  
VRPAALRTA-LGGARGHGGFNSALVVRAGQ-----  
PRTAEVNTA-LVIARGHGGFNSAMVVRSAN-----  
ARPAEPRTA-LVLARGLMGSNSALVLRRAVPPETR-  
AREQRVDIV-LTVGSGFGGFQSAMVLRPEEAA----  
AREQRVDIV-LSVGSGFGGFQSAMVLRRLGGANS---  
ARERKLRSV-LTVGSGFGGFQSAMVLRDAETAGAAA-  
ARDQRVDSV-LTVGSGFGGFQSAMVLTSAQ---RSTV  
CREQLTDSV-LTVGSGFGGFQSAMVLARPE---RKIA  
ARACPVDTV-LTVGSGFGGFQSAMVLCGPGSRGRSAA  
AREQRVDIV-LSVGSGFGGFQSAVLRAPKETRS---  
AREKRVRA-LTVGSGFGGFQSAMLLSRPER-----  
AREKRVRA-LTVGSGFGGFQSAMLLSRLER-----  
ARERTLRHV-LSVGSGFGGFQSAVLSGSEGGLR---  
\* . \* . \* \* ::\* ::

mole:-/ks2%

Fig 2D

## ORGANISATION OF THE TYLOSIN-PRODUCING POLYKETIDE SYNTHASE

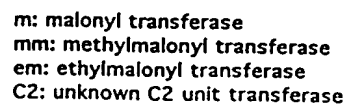


Fig. 4A

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	1					50
niddamycin	-----	-----	MAGHGDATAQ	KAQDAEKSED	GSDAIAVIGM	
platenolide	-----	-----	-----MS	GELAISRSDD	RSDAVAVVGM	
monensin	-----	-----	-----MAAS	ASASPSGPSA	GPDPIAVVGM	
oleandomycin	-----	-----	-----	---MHVPGEE	NGHSIAIVGI	
tylosin	MSSALRRVQ	SNCGYGDLMT	SNTAAQNTGD	QEDVDGPDST	HGGEIAVVGM	
	51					100
niddam...	SCRFPGAPGT	AEFWQLLSSG	ADAVVTAADG	RRR.....	.....GTIDA	
platenol.	ACRFPGAPGI	AEFWKLLTDG	RDAIGRDADG	RRR.....	.....GMIEA	
monensin	ACRLPGAPDP	DAFWRLLESG	RSVSTAPPE	RRRADSGLHG	P...GGYLDR	
oleandom	ACRLPGSATP	QEFWRLLADS	ADALDEPPAG	RFPTGSLSSP	PAPRGGFLDS	
tylosin	SCRLPGAAGV	EEFWELLRSG	RGMPTRQDDG	TWRAA.....	.....LED	
	101					150
niddam...	PADFDAAFFG	MSPREAAATD	PQORLVLELG	WEALEDAGIV	PESLRGEAAS	
platenol.	PGDFDAAFFG	MSPREAAETD	PQORLMLELG	WEALEDAGIV	PGSLRGEAVG	
monensin	IDGFDADFFH	ISPRAVAMD	PQORLLELS	WEALEDAGIR	PPTLARSRTG	
oleandom	IDTFDADFFN	ISPRAEGLD	PQORLLELG	WEALEDAGIV	PRHLRGTRTS	
tylosin	HAGFDAGFFG	MNARQAAATD	PQHRLMLELG	WEALEDAGIV	PGDLTGTDG	
	151					200
niddam...	VFVGAMNDY	ATLLH.RAGA	PTDITYTATGL	QHSMIANRLS	YFLGLRGPSL	
platenol.	VFVGAMHDDY	ATLLH.RAGA	PVGPHATATGL	QRAMLANRLS	YVLGTRGPSL	
monensin	VFVGAFWDDY	TDVLNLRAPG	AVTRHTMTGV	HRSILANRIS	YAYHLAGPSL	
oleandom	VFMGAMWDDY	AHLAHARGE	ALTRHSLTGT	HRGMIANRLS	YALGLQGPSL	
tylosin	VFAGVASDDY	A.VLTRRSV	SAGGYTATGL	HRLAANRLS	HFLGLRGPSL	
	201					250
niddam...	VVDTGQSSSL	VAVALAVESL	RGGTSGIALA	GGVNLVLAEE	GS.AAMERVG	
platenol.	AVDTAQSSSL	VAVALAVESL	RAGTSRVAVA	GGVNLVLADE	GT.AAMERLG	
monensin	TVDTAQSSSL	VAVHLACESI	RSGDSIAFA	GGVNLICSPR	TTELAARFG	
oleandom	TVDTGQSSSL	AAVHMACESE	ARGESDLALV	GGVNLVLDPA	GT.TGVERFG	
tylosin	VVDSAQSASL	VAVQLACESL	RRGETSLAVA	GGVNLILTEE	ST.TVMERMG	
	251					300
niddam...	ALSPDGRCHT	FDARANGYVR	GEGGAIVVLK	PLADALADGD	RVYCVVRGVA	
platenol.	ALSPDGRCHT	FDARANGYVR	GEGGAIVVLK	PLADALADGD	PVYCVVRGVA	
monensin	GLSAAGRCHT	FDARADGFVR	GEGGGLVVLK	PLAAARRDGD	TVYCVIRGSA	
oleandom	ALSPDGRCHT	FDSRANGYAR	GEGGVVVVLK	PTHRALADGD	TVYCEILGSA	
tylosin	ALSPDGRCHT	FDARANGYVR	GEGGGAIVVLK	PLDAALADGD	RVYCVIKGGA	
	301					350
niddam...	TGNDGGGPGL	TVPDRAGQEA	VLRAACDQAG	VRPADVRFVE	LHGTGTPAGD	
platenol.	VGNDGGGPGL	TAPDREGQEA	VLRAACAQAR	VDPAEVRFVE	LHGTGTPVGD	
monensin	VNSDGTDDGI	TLPQGQAQOD	VVRLACRRAR	ITPDQVQYVE	LHGTGTPVGD	
oleandom	LNNDGATEGL	TVPSARAQAD	VLRAQAWERAR	VAPTDVQYVE	LHGTGTPAGD	
tylosin	VNNDGGGASL	TTPDREAQEA	VLRAQAYRRAG	VSTGAVRYVE	LHGTGTRAGD	

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	351				400
niddam...	PVEAEALGAV	YGTGRP..AN	EPLLVGSVKT	NIGHLEGAAG	IAGFVKAALC
platenol.	PVEAHALGAV	HGSGRP..AD	DPLLVGSVKT	NIGHLEGAAG	IAGLVKAALC
monensin	PIEAAALGAA	LGQDAA..RA	VPLAVGSAKT	NVGHLEAAAG	IVGLLKOTALS
oleandom	PVEAEGLGTA	LGTARP..AE	APLLVGSVKT	NIGHLEGAAG	IAGLLKTVLS
tylosin	PVEAAALGAV	LGAGADSGRS	TPLAVGSVKT	NVGHLEGAAG	IVGLIKATLC
	401				450
niddam...	LHERALPASL	NFETPNPAIP	LERLRLKVQT	AHAALQPGTG	GGPLLAGVSA
platenol.	LRERTLPGSL	NFATPSPAIP	LDQLRLKVQT	AAAELPLAPG	GAPLLAGVSS
monensin	IHHRLAPSL	NFTTPNPAIP	LADLGLTVQQ	DLADWP..RP	EQPLIAGVSS
oleandom	IKNRHLPASL	NFTSPNPRID	LDALRLRVHT	AYGPWP..SP	DRPLVAGVSS
tylosin	VRKGELVPSL	NFSTPNPDIP	LDDLRLRVQT	ERQEW.NEED	DRPRVAGVSS
	451				500
niddam...	FGMGGTNCHV	VLEETPGG..	.....	.....	...RQPAE.T
platenol.	FGIGGTNCHV	VLEHLPSR..	.....	.....	...PTPAV.S
monensin	FGMGGTNCHV	VVA....AAP	DSVAVPEPVG	VPERVEVPEP	VVVSEPVVVP
oleandom	FGMGGTNCHV	VLSELRNAGG	DGAGKGPYTG	TEDRLGATEA	EKRDPDPATGN
tylosin	FGMGGTNVHL	VIAEAPAAAG	SSGAGGSGAG	SGAGISAVSG	VV.....
	501				550
niddam...	GQADACLFSA	SPMLLLSARS	EQALRAQAAR	LREHL..EDS	GADPLDIAYS
platenol.	VAAS...LPD	VPPLLLSARS	EGALRAQAVR	LGETV..ERV	GADPRDVAYS
monensin	TPWP.....	.....VSAHS	ASALRAQAGR	LRTHLAAHRP	TPDAARVGHHA
oleandom	GPDPAQDTHR	YPALILSARS	DAALRAQAER	LRHHL.EHSP	GQRLRDTAYS
tylosin	.....	..PVVVSGRS	RVVVREAAGR	LAE..VVEAG	GVGLADVAVT
	551				600
niddam...	LATTRTRFEH	RAAVPCGDPD	RLSSALAALA	AGQTPRGVRI	GS..TDADGR
platenol.	LASTRTLFEH	RAVVPCGGRG	ELVAALGGFA	AGRVSGGVRS	GR..A.VPGG
monensin	LATTRAPLAH	RAVLLGGDTA	ELLGSLDALA	EGAETASIVR	GEAYT..EGR
oleandom	LATTRQVFER	HAVVTGHDRE	DLLNGLRDLE	NGLPAPQVLL	GRTPTPEPGG
tylosin	MAD.RSRFGY	RAVVLARGEA	ELAGRLRALA	GGDPDAGVVT	G...AVLDGG
	601				650
niddam...	LALLFTGQGA	QHPGMGQELY	TDPHFAAAL	DEVCEELQRC	GTQNLREVMF
platenol.	VGVLFTGQGA	QWVGMGRGLY	AGGGVFAEVL	DEVLSMVGEV	DGRSLRDVMF
monensin	TAFLFSGQGA	QRLGMGRELY	AVFPVFADAL	DEAFAALDVH	LDRPLREIVL
oleandom	LAFLFSGQGS	QQPGMGKRLH	QVFPGFRDAL	DEVCAELDTH	LGRL.....
tylosin	VVVGAAAPGA	GAAGGAGAAG	GAGGGGVVLV	FPGQGTQWVG	MGAGLLGSSE
	651				700
niddam...	TPDQPD....	.....	.....	LLDRTEYTQP	ALFALQTALY
platenol.	GDVDVDAGAG	ADAGAGAGAG	VSGSGSVGG	LLGRTEFAQP	ALFALEVALF
monensin	GETDSGGNVS	GENVIGEGA.	.....DHQA	LLDQTAYTQP	ALFAIETSLY
oleandom	.GPEAGPPLR	DVMFAERGT.	.....AHSA	LLSETHYTQA	ALFALETALF
tylosin	VFAASMRECA	RALSVHVGWD	LLEVVSOGGAG	.LERVDVVQP	VTWAVMVSLA
	701				750
niddam...	RTLTARGETQA	HLVLGHSVGE	ITAHHIAGVL	DLPDAARLIT	ARAHVMGQLP
platenol.	RLEARGVEV	SVVLGHSVGE	VAAATVAGVL	SLGDAVRLVV	ARGGLMGGLP
monensin	RLAASFGLKP	DYVLGHSVGE	IAAAHVAGVL	SLPDASALVA	TRGRMLQAVR
oleandom	RLLVQWGLKP	DHLAGHSVGE	IAAAHAAGIL	DLSDAAELVA	TRGALMRSIP
tylosin	RYWQAMGVDV	AAVVGHSQGE	IAAATVAGAL	SLEDAAAVVA	LRAGLIGRYL

Fig 4B

↑

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	751		800
niddam...	HG.GAMLSVQ	AAEHDLDQLA	HTHG..VEIA AVNGPTHCVL SGPRTALEET
platenol.	VG.GGMWSVG	ASESVVRGVV	EGLGEWVSVA AVNGPRSVVL SGDVGVLSEV
monensin	AP.GAMAAWQ	ATADEAAEQL	AGHERHVTVA AVNGPDSVVV SGDRATVDEL
oleandom	GG.GVMLSQ	APESSEVAPLL	LGREAHVGLA AVNGPDAVVV SGERGHVAAI
tylosin	AGRGAMAAVP	LPAGEVEAGL	.AKWPGVEVA AVNGPASTVV SGDRRAVAGY
	801		850
niddam...	AQHLREQNVR	HTWLKVSHAF	HSALMDPMLG AFRDTLNTLN Y..QPPTIPL
platenol.	VASLMGDGVE	YRRLDVSHGF	HSVLMEPVLG EFRGVVESLE FGRVRPGVVV
monensin	TAAWRGRGRK	AHHLKVSHAF	HSPHMDPILD ELRAVAAGLT FHE..PVIPV
oleandom	EQILRDRGRK	SRYLKVSHAF	HSPLMEPVLE EFAEAVAGLT FRA..PTTPL
tylosin	VAVCQAEQVQ	ARLIPVDYAS	HSRHVEDLKG ELERVLSGI. .RPRSPRPV
	851		900
niddam...	ISNLTGQIA.	.....DPNHL	CTPDYWIDHA RHTVRFADAV QTAHHQGT
platenol.	VSGVSGGVV.	.....GSGEL	GDPGYWVRHA REAVRFADGV GVVRLGVGT
monensin	VSNVTGELVT	ATATGSGAGQ	ADPEYWARHA REPVRFLSGV RGLCERGVTT
oleandom	VSNLTG....	..APVDDRTM	ATPAYWVRHV REAVRFGDGI RALGKLGTGS
tylosin	CSTVAGEQPG	EPVF.....	.DAGYWFRNL RNRVEFSAVV GGLLEEGRH
	901		950
niddam...	YLEIGPHPTL	TLLHHTL..	.DNP.....T TIPTLHRERP
platenol.	LVEVGPHGVL	TGMAGECLGA	GDDV.....V VVPAMRRGRA
monensin	FVELGPDAPL	SAMARDCFPA	P.....ADRSRPRPA AIATCRRGRD
oleandom	FLEVGPDGVL	TAMARACVTA	APEPGHRGEQ GADADAHTAL LLPALRRGRD
tylosin	FIEVSAHPVL	V.....	.....HAIEQ TAEAADRSVH ATGTLRRQDD
	951		
niddam...	EPETLTQAIA	AVGVRTDGID	WAVLCGASRP RRVELPTYAF
platenol.	EREVFEEAALA	TVFTRDAGLD	ATALHTGSTG RRIDLPTTPF
monensin	EVATFLRSLA	QAYVRGADVD	FTRAYGATAT RRFPLPTYPF
oleandom	EARSLTEAVA	RLHLHGVPMD	WTSVLGGDVS .RVPLPTYAF
tylosin	SPHRLLTSTA	EAWAHGATLT	WDPAL..PPG HLTTLPTYPF

niddam: niddamycin; platenol: platenolide I (spiramycin); oleandom: oleandomycin.

FIG. 4C

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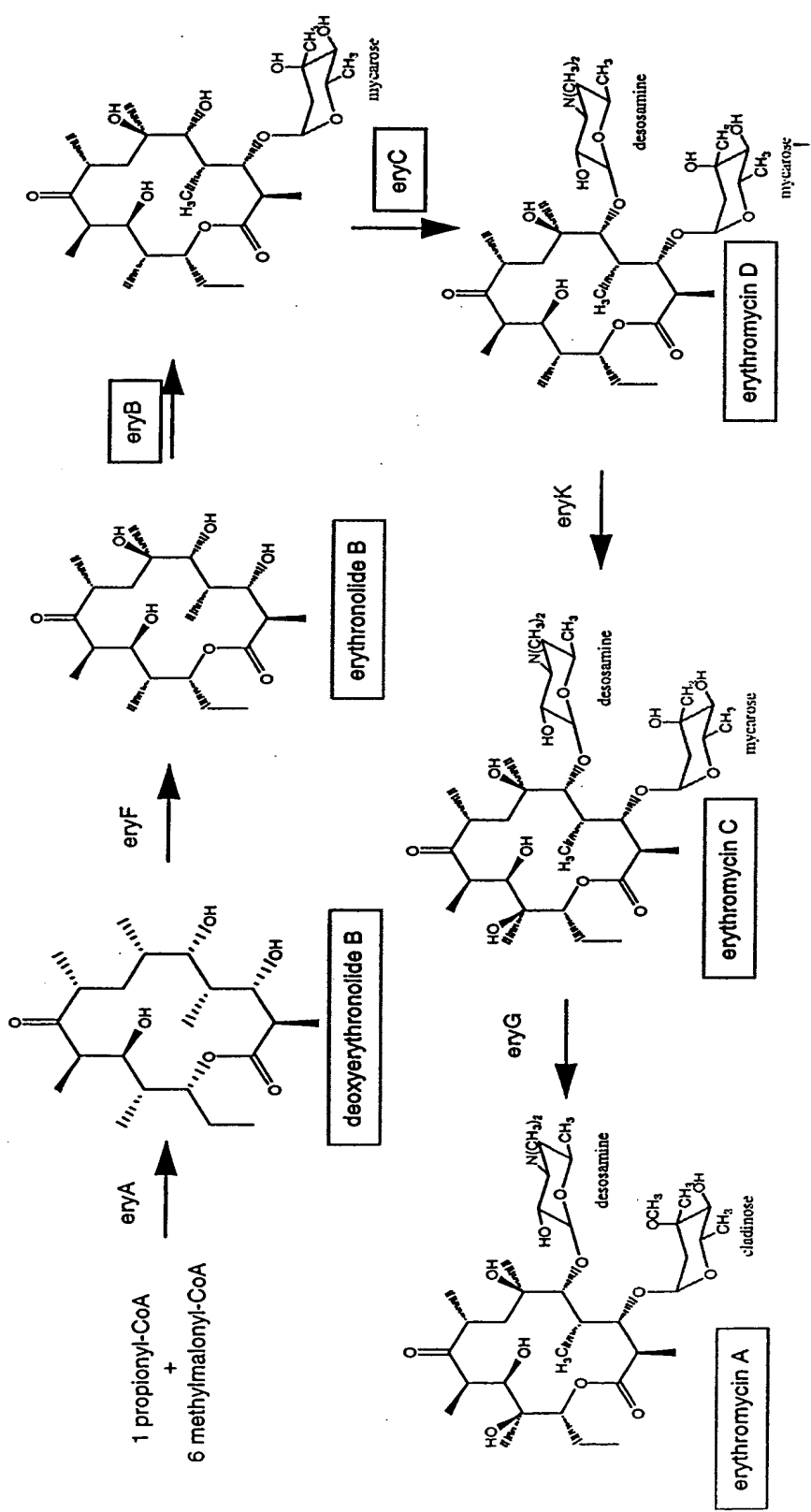


Fig. 5

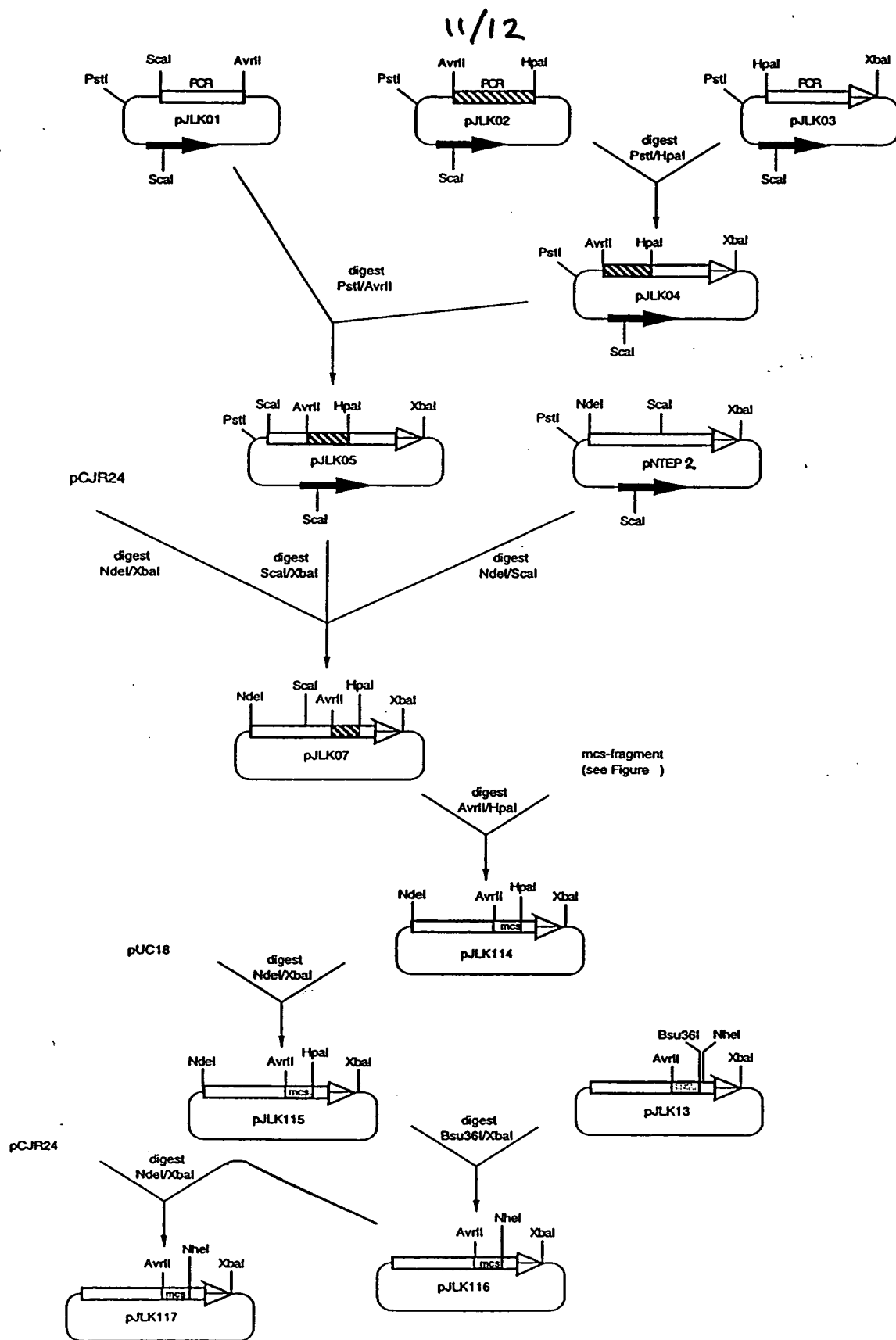


Fig 6

Figure 7

forward (Plf) :

5'-CTA GGC CGG GCC GGA CTG GTA GAT CTG CCT ACG TAT CCT TTC CAG GGC AAG CGG TTC TGG CTG CAG CCG GAC CGC ACT AGT CCT CGT GAC GAG

GGA GAT GCA TCG AGC CTG AGG GAC CGG TT-3'

backward (Plb) :

5'-AAC CGG TCC CTC AGG CTC GAT GCA TCT CCC TCG TCA CGA GGA CTA GTG CGG TCC GGC TGC AGC CAG AAC CGC TTG CCC TGG AAA GGA TAC GTA

GGC AGA TCT ACC AGT CCG GCC CGG C-3'

oligos annealed:

CTAGCCCGGCGGACTGGTAGATCTGCCTACGTATACCTTTCCAGGGCAAGCGGTTCTGGCTGCAGCCGGACCGCACTAGTCTCTGTGACGAGGGAGATCCATCGAGCCTGAGGGACCGGTT  
CGGCGGCGGCGGCTGACCATCTAGACGGATGCAATAGGAAGGTCCCGTTCCCAAGACCGACGTCGGCCTGGCGTGATCAGGAGCACTGCTCCCTCTACGTAGCTCGGACTCCCTGGCCAA  
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AvrII BglII SnaBI PstI SpeI NsiI Bsu36I HpaI  
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